DETAILED ACTION

Status of Claims

1. Claims 1-26 are pending in this application.

2. Claims 3, 15, 17, and 24 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/8/08.

3. Claims 6 and 20 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/8/08.

4. Claims 1, 2, 4, 5, 7-14, 16, 18, 19, 21-23, 25, and 26 are examined.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 2, 4, 5, 7-14, 16, 18, 19, 21-23, 25, and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, as amended, now reads administration of oleuropein as active compound to a subject who is suffering from “unbalanced bone formation/bone

resorption ratio". It is not clear what the metes and bounds are of the phrase, "unbalanced bone formation/bone resorption ratio", since it is not clear what constitutes a "balanced" ratio, and what is meant by "unbalanced" (for example, is the bone formation too high and bone resorption too low, or vice versa, or some other ratio which constitutes "unbalanced"?).

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 2, 4, 5, 7-14, 16, 18, 19, and 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamdi et al (US 2003/0004117).

The claimed invention is drawn to a method for inhibiting bone resorption in humans or animals comprising the administration to a subject in need thereof a composition comprising oleuropein as active compound (see claim 1). Applicants have elected osteoporosis as the disease to be treated (see claim 7).

Hamdi et al teach methods for inhibiting angiogenesis comprising administering oleuropein and/or the products of its hydrolysis in therapeutically effective amounts (abstract). Since oleuropein is present in therapeutically effective amounts, it reads on "active compound." The methods and compositions are particularly effective in inhibiting the vascularization of endothelial cells, and may be utilized to treat a wide

variety of cancers, ocular diseases, and inflammatory conditions (abstract). The populations to which the compositions of Hamdi are administered are the same as those of the claimed invention, since persons being treated for cancers, ocular diseases, and inflammatory conditions would also suffer from unbalanced bone formation/bone resorption ratio (since the bone remodeling process becoming unbalanced appears to be a "universal phenomenon", as described by Applicants at page 2 of the specification), and/or seek to prevent bone loss which occurs with aging, and/or seek to prevent a disorder associated with unbalanced bone formation-bone resorption ratio, and/or might suffer from a condition such as type I or type II osteoporosis or secondary osteoporosis. It is further noted that Hamdi exemplifies a sufficient amount of oleuropein as 0.025 g in a mouse model (see Example 3). Assuming an average weight of 0.02 kg for a lab mouse and 67.5 kg for an average human, this equates to a sufficient amount of oleuropein for a human being 84.3 g, which is within Applicant's range (see claims 14 and 23). Therefore, since the same composition (i.e., a composition comprising oleuropein as active compound) is administered to the same population(s) in the same amount, the same effect(s) would necessarily take place, i.e., stimulation of bone formation and/or inhibition of bone resorption. Therefore, the invention of Hamdi anticipates the claimed invention.

Regarding claims 4, 5, 7, 18, 19, and 21, it is noted that the populations to which the compositions of Hamdi are administered are the same as those of the claimed invention, since persons being treated for cancers, ocular diseases, and inflammatory conditions would also suffer from unbalanced bone formation/bone resorption ratio

(since the bone remodeling process becoming unbalanced appears to be a “universal phenomenon”, as described by Applicants at page 2 of the specification), and/or seek to prevent bone loss which occurs with aging, and/or seek to prevent a disorder associated with unbalanced bone formation-bone resorption ratio, and/or might suffer from a condition such as type I or type II osteoporosis or secondary osteoporosis.

Regarding claims 8 and 9, Hamdi et al teach the compositions may be formulated orally in solid, semi-solid, or liquid form, including powders, slurries, and solutions (see paragraph 74); said forms reasonably read on "a food composition or beverage" in wet or dry form.

Regarding claims 10-13, Hamdi et al teach that the extract may be from olive leaf (i.e., *olea europaea*) (e.g., see paragraph 54).

Regarding claims 14 and 23, Hamdi exemplifies a sufficient amount of oleuropein as 0.025 g in a mouse model (see Example 3). Assuming an average weight of 0.02 kg for a lab mouse and 67.5 kg for an average human, this equates to a sufficient amount for a human being 84.3 g, which is within Applicant’s range.

Regarding claim 16, Hamdi et al teach that a pharmaceutical composition of oleuropein may be administered (paragraph 15).

Regarding claim 22, Hamdi et al teach that the compositions may be in a suitable form for oral, parenteral, intraperitoneal, or intradermal administration (paragraph 74).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 2, 4, 5, 7-14, 16, 18, 19, 21-23, 25, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockwood (US Patent 7,445,807) in view of Nachman (US Patent 5,714,150).

The claimed invention is drawn to a method for inhibiting bone resorption in humans or animals comprising the administration to a subject in need thereof a composition comprising oleuropein as active compound (see claim 1).

Lockwood teaches agglomerated granular protein-rich nutritional supplements formulated to enhance the nutritional intake of various types of persons of disparate ages, genders, and levels of physical activity, comprising edible nutritional food proteins; edible carbohydrates; edible fats; edible dietary vitamins and minerals; edible amino acids; and **edible plant extracts** (col. 8, lines 28-38) which may include olive leaf extract (col. 9, lines 28-37). Olive leaf extract is known to inherently contain oleuropein; as evidence, Nachman teaches a method of producing olive leaf extract known as oleuropein with valuable medicinal properties, including antiviral activity (see abstract and column 1), and therefore reasonably reads on “active compound”. Therefore, one skilled in the art of edible plant extracts would envisage oleuropein from the disclosure

of "olive leaf extract" in Lockwood, and thus the composition of Lockwood reads on “a composition comprising oleuropein as active compound” as taught in claim 1.

While Lockwood teaches a composition comprising edible plant extracts which may be olive leaf extract (which inherently contains oleuropein), Lockwood does not specifically exemplify a composition comprising olive leaf extract sufficient to anticipate the claimed invention. Therefore, the rejection is made under obviousness.

Nachman teaches a method of producing olive leaf extract known as oleuropein with valuable medicinal properties, including antiviral properties (see abstract and column 1).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to select olive leaf extract as the edible plant extract in the composition of Lockwood, since olive leaf extract provides the benefits of valuable medicinal properties, including antiviral properties, as taught by Nachman (abstract and column 1). Therefore, one skilled in the art would be motivated to select olive leaf extract from the list of edible plant extracts taught by Lockwood for inclusion in its composition, in order to improve the overall health of those taking the composition, including persons of disparate ages, genders, and levels of physical activity.

Additionally, while Lockwood does not specifically teach that the supplement comprising olive leaf extract stimulates bone formation and/or inhibits bone resorption, the populations to which the compositions of Lockwood are administered are the same as those of the claimed invention, since all persons of disparate genders, ages, and levels of physical activity would suffer from unbalanced bone formation/bone resorption

ratio (since the bone remodeling process becoming unbalanced appears to be a "universal phenomenon", as described by Applicants at page 2 of the specification), and/or seek to prevent bone loss which occurs with aging, and/or seek to prevent a disorder associated with unbalanced bone formation-bone resorption ratio, and/or might suffer from a condition such as type I or type II osteoporosis or secondary osteoporosis. It is further noted that the amounts of edible plant extracts taught by Lockwood (i.e., 50 mg; see col. 14, line 32) fall within the range taught by the claimed invention (see claims 14 and 23). Therefore, since the same composition (i.e., a composition comprising oleuropein as active compound) is administered to the same population(s) in the same amount, the same effect(s) would necessarily take place, i.e, stimulation of bone formation and/or inhibition of bone resorption.

Regarding claims 2 and 22, Lockwood teaches that the supplement is in oral unit dosage form (abstract).

Regarding claims 4, 5, 7, 18, 19, and 21, Lockwood teaches that the supplements may be used for postmenopausal women which are particularly susceptible to osteoporosis (col. 1, lines 35-38); said women would naturally seek to prevent bone disorders, including bone loss which occurs with aging and disorders associated with unbalanced bone formation-bone resorption ratio. Said women also might suffer from type I or type II osteoporosis or secondary osteoporosis.

Regarding claims 8 and 9, Lockwood teaches that the supplement may be in the form of a rapidly dissolvable wafer or dissolved in a liquid (column 19); said forms reasonably read on "a food composition or beverage" in wet or dry form.

Regarding claims 10-13, Lockwood teaches that the extract may be from olive leaf (i.e., *olea europaea*).

Regarding claims 14 and 23, Lockwood teaches that the supplements for women may comprise 50 mg of edible plant extracts (col. 14, line 32). While Lockwood does not explicitly state that the supplements are administered daily, Lockwood does teach that certain components are formulated according to the Recommended Daily Allowance (for example, see col. 9, lines 5-10), and therefore one skilled in the art would reasonably expect that the supplements are administered daily.

Regarding claim 16, Lockwood teaches that its compositions may comprise olive leaf extract, which is known to have valuable medicinal properties as taught by Nachman, and therefore the composition of the combined references reasonably reads on a pharmaceutical composition.

Regarding claims 25 and 26, Lockwood teaches that the supplement may be in the form of a rapidly dissolvable wafer, including a combination of carbohydrate and non-caloric sugar substitute (col. 19, lines 21-26). Said form reasonably reads on “confectionary product” and “cookie”.

Response to Arguments

11. Applicant's arguments filed 5/16/11 and Declaration filed 7/22/11 have been fully considered but they are not persuasive.

Applicants argue that the Examiner has asserted that because Hamdi’s method might be used on patients who suffered from osteoporosis, it inherently anticipates the

presently claimed invention. However, the rejection does not state an inherency with osteoporosis (see note regarding Allowable Subject Matter, below), but rather that those who seek to prevent such a condition would encompass the population treated by Hamdi. As for Applicant's amendment, it is noted that the bone remodeling process becoming unbalanced appears to be a “universal phenomenon”, as described by Applicants at page 2 of the specification, and therefore the population of the claimed invention still appears to encompass the population of Hamdi. In response to arguments in the Declaration regarding differing and/or unrelated populations, it is noted that, while certain populations of Hamdi may not need to induce bone formation and/or inhibit bone resorption, they would still seek to prevent conditions resulting from unbalanced bone formation/bone resorption ratio and/or would suffer from an “unbalanced bone formation/bone resorption ratio”, and therefore would still encompass the population of Hamdi. Thus, regardless of whether or not the treatment of the diseases of Hamdi occurs by a different mechanism than that of the claimed invention, since the same composition (i.e., a composition comprising oleuropein as active compound) is administered to the same population(s) in the same amount, the same effect(s) would necessarily take place, i.e, stimulation of bone formation and/or inhibition of bone resorption.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was

within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to Applicant's arguments that the edible plant extract of Lockwood may not be present and/or may not contain oleuropein, it is noted that the teachings of Nachman that the olive leaf extract of oleuropein contains antiviral properties would motivate one skilled in the art to include said extract in the supplement of Lockwood in order to improve its medicinal and nutritional value (since a component having antiviral properties would improve the immune function and consequently the overall health of the consumer, which is consistent with the purpose of the nutritional supplement). Therefore, while Declarant's arguments regarding olive leaf extracts have been fully considered, they are not considered sufficient to overcome the obviousness rejection.

In response to Applicant's arguments that the presently claimed invention is not a composition but instead is a method for stimulating bone formation and/or inhibiting bone resorption comprising the administration of oleuropein, it is noted that the teachings of both Hamdi and Lockwood include administration of their compositions to various populations which are encompassed by the population of the claimed invention. Therefore, since the same composition (i.e., a composition comprising oleuropein as active compound) is administered to the same population(s) in the same amount, the same effect(s) would necessarily take place, i.e., stimulation of bone formation and/or inhibition of bone resorption.

Therefore, it is the Examiner's position that the claims are anticipated and/or rendered obvious.

Allowable Subject Matter

12. Subject matter which would be considered for allowability at this time is: the method of claim 1 wherein, instead of administration to a subject in need thereof who is suffering from unbalanced bone formation/bone resorption ratio, the method comprises administration of a composition comprising oleuropein as active compound to a subject in need thereof who is suffering from a condition selected from the group consisting of type I or type II osteoporosis, secondary osteoporosis, Paget's disease, osteolysis observed at the vicinity of a prosthesis, periodontal disease or osteoarthritis.

Conclusion

No claims are allowed at this time.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Joanne Hama/
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